IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Ashkenazi *et al.*	Docket No:	39780-2730P1C65
Serial No:	09/989,727	Group Art Unit:	1647
Filed:	November 19, 2001	Examiner:	Romeo, David

For: **SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME**

DECLARATION OF WILLIAM WOOD, Ph.D.

1. I, William Wood, declare and say as follows:-

2. I am a Director and Staff Scientist in the Bioinformatics Department of Genentech, Inc., South San Francisco, California.

3. I received a B.A. degree from Cornell University, Department of Chemistry in 1970. In 1971, I received a M.A. degree and in 1977 a Ph.D. from Harvard University, Department of Biochemistry and Molecular Biology. From 1978 to 1981 I worked as a staff fellow at the National Institutes of Health, Laboratory of Molecular Biology. I joined Genentech in 1982, where currently, I serve as head of the Bioinformatics Department.

4. As a result of my focus on bioinformatics and computer work, I am very familiar with the various search programs used to perform cluster analysis in nucleic acid and protein databases, and with methods for determining sequence identity between homologous sequences revealed by such searches, all of which have been used by me and others under my supervision to identify nucleic acids encoding novel polypeptides discovered in Genentech's Secreted Protein Discovery Initiative project.

5. I am also familiar with the disclosure of the above-identified U.S. Patent Application, including the discussions on "cluster analysis" especially in Examples 1-3 and Example 118 of the specification. As explained in Example 1 of the specification:

> "The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST databases included public databases (e.g., Dayhoff, GenBank), and proprietary databases (e.g. LIFESEQ^{TM}, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST-2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons with a BLAST score of 70 (or in some cases 90) or greater

that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, WA)."

Using the approaches of ECD homology screening, clustering and assembly of EST fragments from public (e.g., GenBank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, CA) databases, and extension, we identified clusters that contained DNA sequences encoding for full-length secretory polypeptides. These full-length DNA sequences were later isolated and cloned using PCR-based methods and such methods are described in detail in the Examples of the instant specification. Secretory polypeptide-encoding cDNA sequences were further identified in the nucleic acid sequences described above by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, CA). A brief explanation of how the signal sequence finding algorithm identifies a secretory polypeptide-encoding nucleic acid sequence is found in Example 3. Since the signal sequence finding algorithm was proprietary, it was not available to one of ordinary skill in the art.

6. One such cluster of interest that was identified was designated DNA56748. This cluster was found to have some sequence homology with an EST sequence designated as 3476792 in the Incyte SST database, even though the EST 3476792 sequence did not encode for the complete coding sequence of the polypeptide present within DNA56748. This is evident from the alignment between DNA56748 and the EST sequence 3476792 shown in Exhibit A, which is attached and forms part of the present Declaration. For instance, the Incyte EST sequence 3476792 began 68 nucleotides upstream of the first DNA56748 nucleotide but truncated well before the nucleotides encoding for the stop codon of the encoded polypeptide. Thus the Incyte EST 3476792 sequence did not encode for a full-length polypeptide. The EST 3476792 was ordered, and using the methods, including the proprietary methods discussed above, the full-length nucleotide sequence encoding PRO1186 (SEQ ID NO: 371) was determined, cloned and designated as DNA60621 (SEQ ID NO: 370).

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

Dated: 9/28/05

WILLIAM I. WOOD